REMARKS

Claims 1, 60-73 and 79-91 and 97-101 are pending in the application. Claims 2-59, 74-78 and 92-96 have been canceled. Claims 1 and 73 have been amended. Claims 97-101 have been added. Applicants respectfully request reconsideration of the application in view of the following amendment and remarks and the accompanying Declaration under 37 CFR 1.132.

Advisory Action

The Advisory Action mailed February 8, 2005 is acknowledged and addressed by this filing.

Claim Rejections under §112

The withdrawal of the prior rejection of claims 1, 60-73 and 79-91 under 35 U.S.C. §112, first paragraph, for failing to comply with the written description requirement is gratefully acknowledged.

Claim Rejections under §103

The prior rejections under 35 U.S.C. §103(a) were maintained, namely: Claims 1, 60, 61, 63-66, 73, 79, 80, 82-85, 92 and 93 were rejected under 35 U.S.C. §103(a) as being unpatentable over US Patent No. 5,478,527 to Gustafson et al. ("Gustafson") in view of US Patent No. 5,831,070 to Pease et al. ("Pease"). Claims 62 and 81 were again rejected under 35 U.S.C. §103(a) as being unpatentable over Gustafson and Pease and further in view of US Patent No. 6,406,921 to Wagner et al. ("Wagner"). Claims 67-72 and 86-91 were again rejected under 35 U.S.C. §103(a) as being unpatentable over Gustafson and Pease and further in view of US Patent No. 5,482,867 to Barrett et al. ("Barrett").

The pending claims are directed to particular arrays of protein-binding agents stably attached to the surface of a solid support, and kits incorporating such arrays. The arrays and kits are used for conducting proteomic analyses such as differential binding assays in which the binding of a particular protein, that has been labeled with a fluorescent dye, to an array element is detected by a fluorescence-based detection system (see, e.g., page 28, line 3 to page 30, line 13 and page 33, line 32 to page 34, line 7). The arrays are designed to optimize the effectiveness of this fluorescence-based detection system.

The claims have previously been focused on a particular embodiment of the invention in order to expedite prosecution. These claims recite an embodiment of the invention wherein an aluminum on glass substrate surface is coated with a particular configuration of silicon dioxide on the aluminum substrate surface that can amplify the fluorescent signal used to read the arrays

with resultant improvement in performance of the arrays in practice. In particular, a suitable configuration is a thickness of between about 200 and 900Å, and a preferred fluorescent signal generating dye set, the amine reactive dyes Cy3 and Cy5. Claims 1 and 73 have been amended to recite that the solid substrate has a substantially planar surface comprising a layer of aluminum formed on a glass base material, the aluminum coated with a silicon dioxide coating having a thickness of between about 200 and 900Å, and dependent claims 73, and 97-101 and, depending from claims 1 and 73 respectively, have been amended or added to recite the presence fluorescent dye reagents or labeled proteins, and the nature and identity of the preferred fluorescent dyes.

Applicants here reassert the distinction between the array and associated assay technique of the Gustafson reference and that of the presently claimed invention, and the relevance of these distinctions to the patentability of the pending claims. A Declaration under 37 CFR 1.132 of co-inventor Deborah Charych accompanies this response to address issues relating to the optimization of the claimed array substrate for its purpose and the distinct nature of the Gustafson array technology and disclosure relative to the invention described and presently claimed in the application.

Applicants reassert that Gustafson lacks any disclosure of fluorescence signal amplification or its advantages in the context of microarray technology. With regard to the assertion in the Advisory Action that Gustafson provides a teaching with regard to fluorescence signal amplification, Applicants respectfully maintain that this is simply not the case. The Examiner is directed to column 3, line 56 to column 4, line 5 for the description of the biograting and to column 4, lines 6-36 where the terms "binding reagent," "binding assay" and "light disturbing" are defined. Nowhere therein or elsewhere in the application is reference made to fluorescent labels or fluorescent signal detection. The reference simply does not provide any disclosure on this point because its biograting assay is a completely different, and label-free, assay technology. This issue is also addressed by Dr. Charych in her Declaration.

As noted by Dr. Charych, Gustafson is specifically addressed to providing a suitable substrate for its reflective diffraction biograting. In various embodiments, Gustafson describes substrates composed of silicon applied over silicon dioxide (e.g., see Fig. 4) and in which silicon dioxide is applied over a reflective metal deposited on silicon. The objective is to provide an optically flat reflective substrate that apparently enhances reflective diffraction from a biograting formed on the substrate. Since Gustafson's substrate is specifically designed for their biograting immunoassay, and this assay is label free (i.e., it does not make use of fluorescently labeled probes), it is respectfully submitted that a skilled worker in this field at the time that the invention was made would not have been led to the presently claimed invention by Gustafson in combination with the other cited references, namely Pease, Wagner and Barrett. Gustafson's

teaching of the use of a flat substrate of silicon dioxide on reflective metal would have been viewed as specific to their particular label-free assay.

Due to the fact that the Gustafson reference provides no teaching with regard to a suitable array substrate for a fluorescence-based assay, it certainly does not teach optimization of such an array substrate, as claimed. As noted by Dr. Charych in her Declaration, experiments conducted by the applicant and assignee demonstrated the criticality of the claimed sub-range of 200-900Å of silicon dioxide thickness. No other reference cited by the Examiner in rejecting the claims provides this element of the claims. With reference to MPEP section 2144.05, the Declaration of Dr. Charych provides factual support for result-effective variables that have been optimized and shows the criticality of the claimed range of silicon dioxide thickness. As such, it is respectfully submitted that the *prima facie* case of obviousness has been rebutted, that the combined references do not disclose every element of the claims, and that the claims are non-obvious and patentable over the cited art.

In addition, in order to emphasize the fluorescent labeling and detection aspect of the present invention and the fact that the claimed arrays and kits are specifically configured to optimize the signal obtained in a fluorescent labeled protein assay, claim 73 has been amended to recite fluorescent protein label reagents as party of the kit. Also, claim 97 has been added to recite the array of claim 1 with bound fluorescently labeled proteins. These amendments are submitted to provided a further and independent basis for patentability since none of the cited prior art references discloses or suggest a proteomic assay using fluorescently labeled proteins, as claimed. Claims 98-101 have also been added to recite the nature and identity of suitable fluorescent labels. These additional claim elements are respectfully submitted to clearly distinguish the pending claims from Gustafson alone or in combination with other references.

For at least these reasons, it is respectfully submitted that claim1, and corresponding kit claim 73, of the present application are novel and patentable over the cited references. The remaining pending claims depend, directly or indirectly, from claim 1 or 73 and are thus submitted to be patentable for at least the same reasons. As noted above, the new claims 97-101 are submitted to provide an independent basis for patentability. Accordingly, in view of these amendments, remarks and the accompanying Declaration under 37 CFR 1.132, it is respectfully submitted that the presently pending claims are patentable and withdrawal of the rejections under §103(a) is respectfully requested.

Conclusion

Applicants believe that all pending claims are allowable and respectfully request a Notice of Allowance for this application from the Examiner. Should the Examiner believe that a telephone conference would expedite the prosecution of this application, the undersigned can be

reached at (510) 663-1100. If any additional fees are due in connection with the filing of this amendment, the Commissioner is authorized to charge such fees to Deposit Account 500388 (Order No. CHIRP014).

Respectfully submitted,
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